

-- BACKGROUND OF THE INVENTION

1. Technical Field.

This invention relates to cell culture apparatus for growing animal cells in rotating cylinders, or roller bottles.

2. Description of the Background Art. --

Replace the fourth paragraph on page 1 with the following rewritten paragraph:

-- It is essential in such a system to ensure that each vessel is provided with an equal volume of fluid during processing operations. In some systems, for example, US 3,847,749, or WO 96/05285 (EU 0775196), equal fluid distribution is accomplished by means of a multi-channel peristaltic pump, with each vessel being assigned one channel of the pump. Such systems allow the bottles to be processed in situ and in the horizontal position. --

Replace the fifth paragraph on page 1 with the following rewritten paragraph:

-- In other systems, for example US 3,827,943, or US 3,732,149 a drum or rotor housing a plurality of interconnected cylindrical vessels is tilted into the vertical position during

fluid transfer operations, thus allowing the fluid level in each vessel to equalize by gravity. This has the advantage of simplicity over systems that require a separate pumping channel for each vessel. Unfortunately, the existing arrangements of tilting rotor devices require air and fluid connections to be provided at opposite ends of the vessels, and cannot therefore utilize conventional roller bottles which are readily available, sterile irradiated, in standardized sizes. It would be advantageous if this type of apparatus could be adapted to utilize standard roller bottles. --

On page 2, between lines 5 and 6, insert the heading:

-- SUMMARY OF THE INVENTION --

On page 3, between lines 16 and 17, insert the following heading:

-- BRIEF DESCRIPTION OF THE DRAWINGS --.

On page 4, between lines 7 and 8, insert the following heading:

-- DETAILED DESCRIPTION OF THE INVENTION --.

Replace the second paragraph on page 5 with the following rewritten paragraph:

-- During fluid transfer operations, the stack of bottles is vertically inverted, as shown in figure 2. Equal distribution of fluid to all bottles is then assured by equalization of the fluid 5 level via the manifold 7 under the effect of gravity. As an alternative to volume graduations on the snorkel tube as described above, the bottles 1 may be provided with externally printed graduations 9, showing the fluid volume contained therein when the bottle is inverted. --

Replace the last paragraph on page 7 with the following rewritten paragraph:

-- As fluid is transferred into or out of the bottles 1, the gas space above the fluid 5 is vented to atmosphere via the snorkel tubes 4. Equal distribution of fluid 5 between bottles 1 is assured by allowing the levels to equalize under gravity and by equalization of the pressure within the gas space above the fluid 5 by snorkel tubes 4. --

In the claims:

Please amend claims 1-4 and 6-9 as follows:

1. (Amended) Cell culture apparatus comprising a rotor releasably housing a plurality of cell culture vessels/roller bottles and with means provided to allow rotation of the rotor at a controlled speed about a substantially horizontal axis for cell incubation purposes, with further means provided to allow the rotational axis of the rotor and bottles housed therein to be tilted from a substantially horizontal position to a substantially vertical position such that the bottles are in an inverted position with cap ends of the bottles lowermost, each bottle having a body and being provided with a cap on its cap end, each cap being equipped with a fluid supply/drain connection arranged at a lowest point of the cap when the bottle is in the inverted position, a manifold with at least one sealable external connection and a plurality of connections communicating with the fluid supply/drain connection of each bottle cap, each bottle having a snorkel for venting of gas space within the bottle during fluid transfer, each snorkel tube passing upwards through any fluid in its respective bottle when in the inverted position and formed as an internal extension of the cap thereon, each snorkel tube extending into the body of its respective bottle and having an end opening into the body of the bottle at a position clear of any fluid in both the bottle in the substantially vertical and horizontal orientations thereof, each snorkel tube being further provided with micro-porous venting means to atmosphere, whereby fluid transfer into or out of the bottles is

accomplished via the at least one external connection of the manifold whilst the bottles are in the inverted position.

2. (Amended) Cell culture apparatus as claimed in claim 1 in which each snorkel tube is arranged to extend substantially along a central longitudinal axis of its respective bottle.

3. (Amended) Cell culture apparatus as claimed in claim 1 in which each snorkel tube is provided with graduations along a length thereof.

4. (Amended) Cell culture apparatus as claimed in claim 1 in which an end of each snorkel tube opening into its respective bottle is provided with a fluid trap.

6. (Amended) A roller bottle cap for use on a roller bottle having a body and adapted to allow fluid transfer into or out of the bottle whilst the bottle is inverted substantially vertically, the roller bottle cap comprising a fluid supply/drain connection arranged at a lowest point of the cap when the bottle is vertically inverted, with venting of gas space above fluid in the bottle during fluid transfer being provided by a snorkel tube extending upwards through the fluid, the snorkel tube having an end opening into the body of the bottle at a position clear of the fluid therein.

7. (Amended) A roller bottle cap as claimed in claim 6 in which the snorkel tube is arranged to extend substantially along a central longitudinal axis of the bottle.

8. (Amended) A roller bottle cap as claimed in claim 6 in which the snorkel tube is provided with graduations along a length thereof.

9. (Amended) A roller bottle cap as claimed in claim 6 in which an end of the snorkel tube opening into the bottle is provided with a fluid trap.

Abstract:

Delete any existing abstract and insert the following:

-- ABSTRACT OF THE DISCLOSURE

A cell culture apparatus comprises a rotor releasably housing a plurality of cell culture vessels/roller bottles. The apparatus provides for rotation of the rotor at a controlled speed about a substantially horizontal axis and for the rotational axis of the rotor and the bottles housed therein to be tilted to a substantially vertical position in order to allow fluid to be supplied or drain therefrom. Each vessel is provided with a cap equipped with a fluid supply/drain connection arranged


at the lowest point of the cap when the vessel is vertically inverted (as shown in Figure 1). The supply/drain connection of each bottle cap is connected to a manifold that allows the supply or extraction of fluid via a sealable external connection. Venting the gas space within the bottle during fluid transfer is provided by a snorkel tube passing upwards through the fluid, and formed as an internal extension of the bottle cap. The snorkel tube is provided with a micro-porous filter, venting to atmosphere. During cell incubation stages, the assembly of vessels is rotated about a horizontal axis in the known manner. --

REMARKS

This preliminary amendment makes changes to the specification, claims and abstract of the above-referenced patent application to place the application in better form for examination.

Dated: 3/6/2002

Respectfully submitted,

By 
K. Bradford Adolphson
Attorney for Applicants
Registration No. 30,927

WARE, FRESSOLA, VAN DER SLUYS
& ADOLPHSON LLP
Bradford Green, Building Five
755 Main Street, P.O. Box 224
Monroe, Connecticut 06468
Telephone: (203) 261-1234
Facsimile: (203) 261-5676